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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,480	11/15/2005	Henry Nicolas Jabbour	20747/210	6559

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EXAMINER	
SZNAIDMAN, MARCOS L	
ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,480	JABBOUR ET AL.	
	Examiner	Art Unit	
	MARCOS SZNAIDMAN	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,9,12,13 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-5, 9, 12-13 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to applicant's reply filed on February 26, 2009.

Receipt of Declarations under 37 CFR 1.132 is acknowledged.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Status of claims

Addition of new claim 32 is acknowledged.

Claims 1, 3-5, 9, 12-13 and 32 are currently pending and are the subject of this office action.

Claims 1, 3-5, 9, 12-13 and 32 are presently under examination.

Priority

The present application is a 371 of PCT/GB03/01521 filed on 04/10/2003, which claims priority to foreign application: United Kingdom 0208785.6 filed on 04/17/2002.

Rejections and/or Objections and Response to Arguments

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated (Maintained Rejections and/or Objections) or newly applied (New Rejections and/or Objections, Necessitated by Amendment or New Rejections and/or Objections not Necessitated by Amendment). They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112 (Maintained Rejection)

Claims 1, 3-5, 9, 12-13 and new claim32 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

The reasons for this rejection have been provided in the previous office action dated January 29, 2008, the text of which is incorporated by reference herein.

Applicant's arguments have been fully considered but are not persuasive.

Applicant arguments are similar to the ones previously presented: in the 1.132 declaration and in its remarks, Applicant argues that the specification provides enough data to overcome the enablement rejection. Specifically, Applicants lists all the mechanistic reasons that support their claim that " FP receptor antagonists can treat a female individual for a pathological condition of the uterus associated with abnormal growth of cells of the myometrium or endometrium, including uterine carcinoma,

endometriosis and fibroids". These mechanistic reasons are: 1- the discovery for the first time that there is a higher level of expression of the FP receptor in the uterus during the proliferative phase of the endometrium in the menstrual cycle and that expression in uterine carcinoma tissue is significantly elevated compared with normal uterine tissue, 2- there is elevated expression of the FP receptor in pathological conditions of the uteru,s 3- In Dr. Jabbour declaration and in the Sales reference (Cancer. Res. (20025) 65:7707-7716) it is shown that elevated FP receptor and VEGF expression are co-localized in glandular and epithelial cells lining the blood vessels in endometrial (uterine) adenocarcinomas, and 4- PGF2alpha (the natural ligand of the FP receptor) can cause rapid transphosphorylation and activation of the EGF receptor, and activation of MEK signaling via the FP receptor, resulting in an increase in VEGF promoter activity, expression of VEGF mRNA and secretion of VEGF protein, all of which are consistent with a role for the FP receptor in stimulating blood vessel formation (angiogenesis) in endometrial (uterine) cancer.

These effects of PGF2alpha on the FP receptor could be abolished by treatment of cells with specific FP receptor antagonist, AL8810, and similar effects were found when endometrial adenocarcinoma explants were treated with AL8810.

Examiner's response: all the above arguments only prove that the FP receptor might play a role in the diseases of the uterus claimed by applicant (uterine cancer, fibroids and endometriosis), and definitively is an invitation for further research in this area. However, these arguments do not demonstratel that an FP receptor antagonist could treat any of these diseases. There is no *in-vitro* or *in-vivo* data and/or proof of

mechanism in the instant application and in the literature of any kind to suggest that an FP antagonist might be useful in the treatment of uterine cancer, fibroids and endometriosis.

MPEP 2164.03 cites: "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling. >See, e.g., Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004) ("Nascent technology, however, must be enabled with a specific and useful teaching.' The law requires an enabling disclosure for nascent technology because a person of ordinary skill in the art has little or no knowledge independent from the patentee's instruction. Thus, the public's end of the bargain struck by the patent system is a full enabling disclosure of the claimed technology." In the instant case there is nothing in the prior art suggesting that FP antagonists have any effect on treating a pathological condition of the uterus like uterine carcinoma, endometriosis or fibroids. While it is understood that the absence of working examples should never be the sole

reason for rejecting a claims as being broader than an enabling disclosure, the criticality of working examples in an unpredictable art, such as the treatment of a pathological condition of the uterus like uterine carcinoma, endometriosis or fibroids, is required for practice of the claimed invention. Applicant did not provide a single cell assay that shows that any FP antagonist could prevent or ameliorate the proliferation of a cancerigenous cell. Applicant has provided mechanistic data, that although scientifically relevant, it is not sufficient, for patentability purposes, to establish a correlation with the anticancer activity of FP antagonists. Cancer is a very complex disease that involves several mechanisms, and although one mechanism might have more preponderance over the other, the literature is full of examples of mechanistic approaches that seemed "reasonable and promising" but ultimately failed to prove any utility in fighting any type of cancer. Although the USPTO does not require the same level of data as the FDA, as discussed above, there is a minimum of data that applicant has to provide in order to enable the invention, and the data required is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In this case the amount of knowledge is low and the unpredictability is very high.

As mentioned before, the data provided by Applicant in the specification and the 1.132 declaration, although of scientific relevance, it is an invitation for further research in this area.

With the high level of uncertainty in the area of cancer treatment in general, and since neither the prior art nor the instant application provides any relevant data (except for the mechanistic aspects discussed above) that will suggest that FP antagonist can

treat a pathological condition of the uterus like uterine carcinoma, endometriosis or fibroids, the skilled in the art will have to engage in undue experimentation in order to use the present invention.

Finally, new claim 32 does not solve any of the above issues. Claim 32 introduces new mechanistic aspect of the FP antagonists that do not cure the above discussed deficiencies.

Conclusion

No claims are allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1612
April 20, 2009.

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612